UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/990,091 | 11/21/2001 | Joseph M. Fernandez | INVIT1120-3 | 1288 |

7590 07/07/2003

LISA A. HAILE, Ph.D.
GRAY CARY WARE & FREIDENRICH LLP
Suite 1100
4365 Executive Drive
San Diego, CA 92121-2133

| EXAMINER |
|---|
| WESSENDORF, TERESA D |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1639 | 21 |

DATE MAILED: 07/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/990,091 | FERNANDEZ ET AL. | |
| | Examiner | Art Unit | |
| | T. D. Wessendorf | 1639 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *5/12/03 (telephonic interview)* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *47,57,59-63,71-73 and 76* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *47,57,59-63,71-73 and 76* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☒ Interview Summary (PTO-413) Paper No(s). *21* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

**DETAILED SUPPLEMENTAL ACTION**

This Office action supplements the Office action of 5/1/03, as indicated in the Interview Summary Record.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 47, 57, 59-63, 71-73 and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harney (U.S. 6,277,632) in view of Shuman (U.S. 5,766,891) or Ringrose et al (Eur. J. Biochem.) and Dubensky et al (U.S. 6,342,372).

Harney discloses at col. 1, line 50 up to col. 13,line 18 a method for preparing multicomponent nucleic acid constructs comprising: (a) providing the nucleic acid components and optionally a linking nucleic acid molecule to be assembled into the construct, each nucleic acid component comprising a double stranded nucleic acid molecule having at least one single stranded 5' or 3' terminal sequence, the terminal sequence having sufficient complementarity to either a terminal sequence

in a separate nucleic acid component or to a sequence in a linking nucleic acid molecule so as to allow for specific annealing of complementary sequences and linkage of the components in a predetermined order; (b) incubating the nucleic acid components under conditions which allow for the specific annealing and linkage of the nucleic acid components to thereby produce the nucleic acid multicomponent construct. See the Examples for a detail description of the method and the components used in the method. Harney uses ligase to link the nucleic acid components of the vectors, not vaccinia topoisomerase or integrase/recombinase and does not disclose the Kozak sequence, CACCATG, as claimed However, Shuman discloses topoisomerase-based cloning at col. 7,lines 45-67. Shuman discloses that Topoisomerase-based cloning has several advantages over conventional ligase-based cloning of PCR products. First, the topoisomerase procedure circumvents any problems associated with addition of nontemplated nucleotides by DNA polymerase at the 3' end of the amplified DNA. Second, in topoisomerase-mediated cloning, the only molecule that can possibly be ligated is the covalently activated insert and the insert can only be transferred to the vector. There is no potential for in vitro covalent closure of the vector itself,

which ensures low background. There is also no opportunity for the inserts to ligate to each other (this can be guaranteed by using 5'-phosphate-terminated PCR primers), which precludes cloning of concatameric repeats. Third, there is no need to consider the sequence of the DNA being amplified in designing the PCR primers. It is commonplace in standard cloning to introduce a restriction site into the PCR primer and to cleave the PCR products with that restriction enzyme to facilitate joining by ligase to vector.

Ringrose et al discloses at page 911, paragraph bridging col. 1 and col.2 that FLP and Cre have been used extensively in a variety of organisms to engineer specific DNA rearrangement at defined sites. The recombinase system is also useful in that the inverted-repeat target site, like the FLP and Cre, can be read in both orientations without encountering a stop codon, a feature which is necessary if the site is to be placed in an ORF.

Dubensky, Jr. et al discloses at col. 90, lines 46-58 an oligonucleotide primer sequence comprising the CACCATG sequence (Seq. ID. 69) which are the sequences surrounding the ATG start codon from bases -9 to +1 that conform to the Kozak consensus sequence for efficient translational initiation (Kozak, Cell 44:283-292, 1986).

Accordingly, it would have been obvious to one having ordinary skill in the art to replace the ligase enzyme in the method of Harney with topoisomerase or recombinase as taught by Shuman or Ringrose. One would have been motivated to use topoisomerase or recombinase for the advantages obtained in the used of these enzymes as taught by Shuman and Ringrose. Furthermore, it would have been obvious to use a primer comprising of the known Kozak sequence, CACCATG, in the method of Harney, as this Kozak sequence provides for efficient translation as taught by Dubensky.

***Conclusion***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

De Boer et al (U.S. 6,248,543) discloses, like Dubensky above, the use of the known Kozak primer sequence for efficient translation.

The indicated allowability of the above claims is regretted and withdrawn in view of the following rejections above.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to T. D.

Wessendorf whose telephone number is (703) 308-3967. The examiner can normally be reached on Flexitime.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (703) 306-3217. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-7924 for regular communications and (703) 308-7924 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

T. D. Wessendorf
Primary Examiner
Art Unit 1639

tdw
June 30, 2003